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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,663	11/07/2001	Hendrik J. Schuurman	4-30957A/C1(B/+)	4616

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EXAMINER	
SCHWADRON, RONALD B	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,663	SCHUURMAN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6,10 and 11* is/are pending in the application.

4a) Of the above claim(s) *6 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election without traverse of Group I in the reply filed on 12/2/2004 is acknowledged.

2. Claims 6-9,11 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/2/2004.

3. Claims 1-3,5,10 are under consideration.

4. The abstract of the disclosure is objected to because it does not disclose the claimed invention (eg. the composition of claim 1). Correction is required. See MPEP § 608.01(b).

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3,5,10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabling for the claimed composition for treatment or prevention of xenograft transplant rejection. The specification does not disclose how to use the instant invention for the in vivo treatment of xenograft rejection in mammals including humans. Applicant has not enabled the breadth of the claimed invention in view of the teachings of the specification because the use for the instant invention disclosed in the specification is the in vivo treatment of xenograft rejection in mammals including humans. The state of the art is such that is unpredictable in the absence of appropriate evidence as to how the instant invention could be used for the in vivo treatment of xenograft rejection in mammals including humans.

Judge Lourie stated in Enzo Biochem Inc. v. Calgene Inc. CAFC 52 USPQ2d 1129 that:

The statutory basis for the enablement requirement is found in Section 112, Para. 1, which provides in relevant part that:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same. . . .

35 U.S.C. Section 112, Para. 1 (1994). "To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.' " Genentech, Inc. v. Novo Nordisk, A/S , 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright , 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). Whether claims are sufficiently enabled by a disclosure in a specification is determined as of the date that the patent application was first filed, see Hybritech, Inc. v. Monoclonal Antibodies, Inc. , 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), which in this case is October 20, 1983 for both the '931 and '149 patents.

We have held that a patent specification complies with the statute even if a "reasonable" amount of routine experimentation is required in order to practice a claimed invention, but that such experimentation must not be "undue." See, e.g., Wands , 858 F.2d at 736-37, 8 USPQ2d at 1404 ("Enablement is not precluded by the necessity for some experimentation . . . . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' ") (footnotes, citations, and internal quotation marks omitted). In In re Wands , we set forth a number of factors which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows:

(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737, 8 USPQ2d at 1404. We have also noted that all of the factors need not be reviewed when determining whether a disclosure is enabling. See Amgen, Inc. v. Chugai Pharm. Co., Ltd. , 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends on the facts.").

Regarding Wands factors 4,5,7,8, the instant invention deals with a composition for treating xenograft rejection. Xenotransplantation is the transplantation of organs from one species to a different species. The claimed composition recites that it is used to treat or prevent xenograft rejection. The substantial/real life use for the claimed invention is xenotransplantation in humans. **Adachi** et al. disclose that clinical xenotransplantation has been rarely attempted in humans (see page 1145, first column, first paragraph). In fact, there are tens of thousands of allograft transplants performed each year in the world (eg. human kidney or heart or liver into human recipient) wherein graft survival of multiple years is routinely achieved. Xenotransplantation is currently not used in humans. Thus, the state of the art is that it is highly unpredictable whether any particular method can be used to successfully achieve xenograft transplantation in humans. As per Wands factor (8), the claims encompass the treatment of human disease using the claimed composition.

Regarding Wands factors 1-3, the specification discloses experimental data from experiments performed in rats. However, regarding the xenotransplant rat data disclosed in the specification, **Hasan** et al. disclose that: "The extrapolation of results from rodents to clinical practice is ill advised, yet the data reported here do suggest that similar studies in primates need to be undertaken to establish the possibility of using this clinically applicable therapy to prevent xenograft rejection in man."(page 411, last sentence). Thus, Hasan et al. establishes that is unpredictable based on the rodent data disclosed in the specification as to whether the claimed invention could be used to treat xenotransplantation. In addition, **Tueveson** et al. teach that one problem with rodent models of transplantation is that rejection is easily overcome in said models in comparison to the difficulty of overcoming allograft rejection in humans (see page 100, first full paragraph). Tueveson et al. also teach that, "However, today's small animal models seem to be insufficient to produce data for clinical decision-making." (page 101, second paragraphe). Kahan teaches that,

"Furthermore the improved transplant outcome consequent to CsA introduction demands careful clinical trial methodology to establish the role of new immunosuppressive agents."(page 46, last section). **Kahan** teaches that, "In spite of the abundant transplantation data which establish the synergistic effects of immunosuppressive drug combinations in experimental animals, the concept remains an untested premise in human subjects."(page 43, top paragraph).

Regarding Example 1 in the specification, no experimental data regarding the experiments has been supplied (eg. number of animals used, controls, actual survival time of grafts, information regarding how graft survival was evaluated, etc). Thus, it is not possible to evaluate the relevance of said experiments to the issues under consideration. In addition, said experiments do not use the claimed invention (eg. they use treatment with cyclophosphamide and methylprednisolone, wherein said ingredients are not part of the claimed composition). Furthermore, said experiments do not even use rapamycin. Also, said experiments use a hDAF transgenic organ wherein the results are therefore not necessarily relevant to xenotransplantation per se.

Regarding Example 3 in the specification, no experimental data regarding the experiments has been supplied (eg. number of animals used, controls, actual survival time of grafts, information regarding how graft survival was evaluated, etc). Thus, it is not possible to evaluate the relevance of said experiments to the issues under consideration. In addition, said experiments do not use the claimed invention (eg. they use treatment with cyclophosphamide and methylprednisolon, prednisolon) wherein said ingredients are not part of the claimed composition. Said experiments also require an immunoadsorption step. Furthermore, said experiments do not even use rapamycin. Also, said experiments use a hDAF transgenic organ wherein the results are therefore not necessarily relevant to xenotransplantation per se.

Regarding Wands factor 6, the relative skill of those in the art is high (eg. Ph.D. or M.D.).

It appears that undue experimentation would be required of one skilled in the art to practice the instant invention using the teaching of the specification. See In re Wands 8 USPQ2d 1400(CAFC 1988).

7. Claims 1-3,5,10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 U.S.P.Q.2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the applicant had possession at the time of invention of claimed invention.

The claims recite use of a derivative of rapamycin. The specification does not specifically define what derivative means in the context of rapamycin. In its broadest interpretation, said term would encompass a vast collection of immunosuppressive molecules with little or no structural similarity to rapamycin wherein said molecules were not known or describe in the specification or prior art. Thus, the written description provided in the specification is not commensurate with the scope of the claimed inventions. In view of the aforementioned problems regarding description of the claimed invention, the specification does not provide an adequate written description of the invention claimed herein. See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1404-7 (Fed. Cir. 1997). In University of California v. Eli Lilly and Co., 39 U.S.P.Q.2d 1225 (Fed. Cir. 1995) the inventors claimed a genus of DNA species encoding insulin in different vertebrates or mammals, but had only described a single species of cDNA which encoded rat insulin. The court held that only the nucleic acids species described in the specification (i.e. nucleic acids encoding rat insulin) met the description requirement and that the inventors were not entitled to a claim encompassing a genus of nucleic acids encoding insulin from other vertebrates, mammals or humans, id. at 1240. The Federal Circuit has held that if an inventor is "unable to envision the detailed constitution of a gene so as to distinguish it from other materials. . .conception has not been achieved until reduction to practice has occurred", Amgen, Inc. v. Chugai Pharmaceutical Co, Ltd., 18 U.S.P.Q.2d 1016 (Fed. Cir. 1991). Attention is also directed to the decision of The Regents of the University of California v. Eli Lilly and Company (CAFC, July 1997) wherein is stated: The description requirement

of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. See Fiers, 984 F.2d at 1171, 25 USPQ2d at 1606.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 1,2 are rejected under 35 U.S.C. 102(e) as being anticipate by Nadler (US Patent 5,962,425) as evidenced by DermNet NZ.

Nadler discloses a composition comprising cyclosporin, rapamycin and mycophenolate mofetil (see column 14, lines 45-51). It is an inherent property of mycophenolate mofetil that it is a salt of mycophenolic acid (see DermNet NZ, page 1, line 1). The recitation of an intended use carries no patentable weight in this composition claim. The components of the composition would have to be separate or together. The composition of claim 2 encompasses either.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 1-3,5,10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nadler (US Patent 5,962,415) in view of Haeberlin et al. (WO 97/38689).
Nadler teaches a composition containing cyclosporin, rapamycin and mycophenolate mofetil (see column 14, lines 45-51). The recitation of an intended use carries no patentable weight in this composition claim. The components of the composition would have to be separate or together. The composition of claim 2 encompasses either. Nadler et al. do not teach the claimed kit or composition of claim 5 or 10. Haeberlin et al. teach MPA sodium salt formulated as an enteric coated solid oral dosage form and the advantages of said form of MPA (see pages 1 and 2). The composition in unit dosage form (as per page 2, lines 16-18) would come in a package with instructions, which would constitute the claimed kit. Regarding the particular instructions for use as per claim 5, the particulars of the instructions would carry no patentable weight (see In re Ngai, 70 USPQ2d 1862 (CA FC 2004)). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed inventions because Nadler teaches a composition containing cyclosporin, rapamycin and mycophenolate mofetil whilst Haeberlin et al. teach MPA sodium salt formulated as an enteric coated solid oral dosage form and the wonderful advantages of said form of MPA and the composition in unit dosage form would come in a package with instructions, which would constitute the claimed kit. One of ordinary skill in the art would have been motivated to do the aformentioned because Haeberlin et al. teach MPA sodium salt formulated as an enteric coated solid oral dosage form and the advantages of said form of MPA (see pages 1 and 2).

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600